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"Cortical Substrate of Haptic Representation"

FINAL PROGRESS REPORT TO THE OFFICE OF NAVAL RESEARCH

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The focus of our research has been on the role and mechanisms of *memory in motor control*. Based on our experience and data from primates, we have developed computational *models* of short-term active memory. Such models may have technological interest and applications because this kind of memory is an essential feature of any motor control system, biological or mechanical. As far as I know, the *neurally based and neurally testable* modeling of the function of memory networks is unique among ONR-sponsored programs.

Research in our laboratory led to the discovery of *memory cells* in the cerebral cortex of the monkey. Over a period of several years, extensive studies of neuronal activity and reversible--cryogenic--inactivation in monkeys performing memory tasks have provided us with a theoretical framework of perceptual memory. Within that framework, memory cells are the constituents of widely distributed *cortical networks* which, by mechanisms yet unknown, are activated above certain thresholds and kept active, for seconds or minutes, to retain information for prospective motor action.

In the course of this research we have developed an unusual combination of methods that now make it possible to construct and to test *empirical* models of active

memory. As might be expected, this has aroused the interest of computer scientists, physicists and engineers, and has led to productive collaborations with some of them. One such collaboration was established with David Zipser and his group at UCSD. A second is now underway with Gordon Shaw (UCI, Physics). Collaboration with other scientists (e.g., C. Koch, Caltech) also appears likely.

Our work has three closely interlinked components: (1) Acquisition of *normative neuronal data* of active memory in the monkey; (2) Based on these data, *computer simulation* of the architecture and functional algorithms that govern the activation of a memory network; and (3) *empirical testing* of model-derived predictions by *on-line* analysis of spike trains from activated memory networks. Here are some highlights of accomplishment, in the three research components, during the past four years:

1. "Correlational" neuron-behavior research is important. Without it, we would not have reached our present computational stage, nor would we have the means in the future to evaluate, modify or change our models with any degree of confidence or sophistication. In recent years, we have studied the neuronal correlates of active perceptual memory of two modalities: vision and touch. Neurons in the inferotemporal cortex of the monkey have been found to select (i.e., "attend to"), and to *retain in short-term memory*, certain features of complex visual stimuli (Fuster, 1990). Among other interesting things, inferotemporal cells have revealed the operation of a *gate to memory*, as indicated by their temporary inhibition before the loading of information into

memory. They have also revealed a variety of temporal patterns of discharge during active visual memory. Furthermore, using an automated apparatus for testing *haptic* memory (i.e., memory of objects perceived by active touch), we have also found tactile memory cells in parietal cortex. Surprisingly, we have not only found such cells in parietal association cortex but in *primary somatosensory (SI) cortex* (areas 3, 1, and 2). This may be so because haptic perception, unlike vision, depends heavily on temporal integration, serial processing and, of course, short-term memory. In any event, the temporal patterns of spike frequency in haptic memory cells differ in several respects from those of visual memory cells.

2. About three years ago we initiated our efforts to *model active cortical memory.* We began such efforts in collaboration with Zipser and his colleagues, using as the data base the *visual-memory cells* of my normative study of inferotemporal cortex (Fuster, 1990). For our purpose, we trained computer networks following Zipser's procedure of *neural system identification.* This is basically an optimization procedure ensuring that a network will self-adjust synaptic weights to reproduce a certain input-output relationship. To accommodate the characteristics of inferotemporal memory cells we introduced certain features in our models, such as the conditional role of a *load signal* to take the place of our hypothetical gate; in the brain, that gate may in fact be represented by prefrontal input to inferotemporal cells, since the cortex of the frontal lobe, which is ultimately responsible for organizing behavioral action in the time domain, determines what is to be retained for that action (our first memory cells were discovered in

prefrontal cortex). Other features of our initial models are the spiking character of input and output signals, and the presence of noise. A spiking model with these characteristics has turned out to account remarkably well for the ... of real neurons in active memory (Zipser, et al. 1993). Under a wide range of parameters, the observable "hidden units" of this model mimic with astonishing realism the temporal patterns of inferotemporal cells in active memory. Hidden units can thus be seen to fall within the same basic categories as inferotemporal cells in the monkey. Furthermore, hidden units revealed periodic switching between *attractor frequencies*, a feature which we *post hoc* searched for, and *found*, in the real data. In summary, the exciting conclusion is that a trained model with pre-established and fixed weights can explain the behavior and function of neurons in *active short-term memory*. (Our studies have nothing to do with learning or acquisition of memory; both our monkeys and our networks are thoroughly trained for their task.) But our spiking model is still imperfect in many ways. It does not seem to accommodate haptic memory cells quite as well as visual memory cells. In the future we intend to perfect it and to test it against such cells; this is a problem of particular interest because of the critical importance of haptic memory in motor control. We also intend to develop and test alternate models of active memory--with different architectures--not only in vision and haptics, but in audition as well.

3. All our models so far, as several others in the literature, share one essential feature: *re-entry* or recurrence of impulses between and within the interconnected cell assemblies of a network. It is an old concept, with a firm neuroanatomical base, that would explain the persistent activation of any theoretical or real network. But, in fact,

there is practically no functional evidence for it. It is for this reason that in the past three years we have made a concentrated effort to acquire the technical ability to record and analyze several spike trains simultaneously. Thanks to a grant from the National Science Foundation, and with the help of our UCLA engineers, we have developed an electromechanical system to do it in the awake and behaving monkey. It is a *system of multiple, independently and remotely driven microelectrodes* under computer control. Whereas our system seems quite elaborate, it is considerably simpler and more versatile than the other one we know to exist for use in the awake monkey (developed in Germany for Mountcastle and his colleagues). Consequently we now have for our research two advantages we did not have before: (a) the capability to crosscorrelate spike trains and thus to expose functional relationships *between elements of a network*; and (b) the capability to *move electrodes in accord with the results of immediate on-line time-series analysis*. The system will allow the testing of predictions of functional interaction deriving directly from our models, in particular the principles and characteristics of impulse recurrence in active memory. At some future date we plan to complement the use of our new system with the reversible inactivation (by cooling) of selected portions of a given cortical network (e.g., dorsolateral prefrontal cortex), and thus to study the effects of such inactivation on both behavioral memory performance and the behavior of memory cells.

In summary, our recent research stems from our previous neurobiological work on primate memory. It is on that empirical work that our current theoretical efforts are

founded. Our future physiological research will be based on the results of these theoretical efforts and designed to substantiate them.

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